Cystic fibrosis is an autosomal recessive genetic disease caused by defective salt and water transfer across the cells of the lung and other organs. The disease affects the lungs, digestive system, and sweat glands, as well as other exocrine glands, such as the lacrimal glands and salivary glands. The greatest pathology occurs in the lungs where dysfunction of small airways and recurrent infections cause progressive obstructive pulmonary disease, hypoxemia, and eventually carbon dioxide retention, right ventricular failure, and death. The isolation of the gene for cystic fibrosis (the CFTR gene) has led to the possibility of correcting chloride secretion in the lungs of these patients with normalization of airways function. In this protocol, we propose to evaluate the safety and efficacy of gene therapy in cystic fibrosis using a recombinant adenovirus that is made replication deficient by deletion of the E1 region. It will be used to deliver the CFTR cDNA to the nose, trachea, and one lobe of adult cystic fibrosis patients with mild to moderate disease. We propose to study the safety and efficacy of three different doses of this construct in groups of five patients. The patients will be treated with the ad-CFTR construct and followed for evidence of gene expression, evidence of correction of physiological function of cells, and evidence of improvement in salt transport and mucous clearance in the treated regions of the lung. Patients will be studied for adverse reactions to the virus, duration of the expression of the gene, duration of correction of function, and immunological responses to the construct.